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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,296	06/28/2004	Yuji Yamazaki	081356-0218	7715

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EXAMINER	
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ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,296	YAMAZAKI ET AL.	
	Examiner	Art Unit	
	Zachary Skelding	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6 and 20-25* is/are pending in the application.

4a) Of the above claim(s) *1,2,4 and 6* is/are withdrawn from consideration.

5)☒ Claim(s) *20 and 21* is/are allowed.

6)☒ Claim(s) *22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks filed July 30, 2007 are acknowledged.

   Claims 6, 22, 23 and 25 have been amended.

   Claims 3, 5 and 7-19 have been canceled.

   Claims 1, 2, 4, 6 and 20-25 are pending.

   Claims 1, 2, 4 and 6 have been withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being directed to a non-elected Species.

   Claims 20-25 are under examination as they read on "anti-FGF-23 antibodies that bind amino acid 25-179 of SEQ ID NO:1".

2. This Office Action is in response to applicant's amendment and remarks filed July 30, 2007.

   The prior rejection under 35 U.S.C. § 112, 1st paragraph put forth in the Office Action mailed January 30, 2007 is withdrawn in view of applicant's amendment to the claims.

   The prior rejection under 35 U.S.C. § 102(a) put forth in the Office Action mailed January 30, 2007 is withdrawn in view of applicant's argument.

3. With respect to claims 1, 2, 4 and 6 which were withdrawn in the Office Action mailed January 30, 2007, applicant argues that these claims were prematurely withdrawn.

   Applicant's argument is not found convincing in that as put forth in the Office Action mailed January 30, 2007, and as is made clear in the Restriction Requirement of October 12, 2006, an antibody raised against 180-194 or between 237-251 of SEQ ID NO:2 is a different species from an antibody that binds amino acids 25-179 of SEQ ID NO: 2. According to MPEP § 821, "All claims that the examiner holds as not being directed to the elected subject matter are withdrawn from further consideration by the examiner in accordance with 37 CFR 1.142(b)."

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

   A person shall be entitled to a patent unless –

   (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 23-25 stand rejected under 35 U.S.C. § 102(b) as anticipated by Itoh et al. (WO 01/66596, cited on applicant's IDS of June 28, 2004), as evidenced by Yu et al. (Endocrinology. 2005 Nov;146(11):4647-56) and Mohammadi et al. (Cytokine Growth Factor Rev. 2005 Apr;16(2):107-37), essentially for the reasons of record as put forth in the Office Action mailed January 30, 2007.

Applicant argues that "Itoh does not teach or suggest that antibody against amino acids 1-179 can neutralize FGF-23 activity, as claim 23 prescribes," and therefore the cited reference does not teach all elements of the claimed invention.

Applicant's arguments have been considered, but have not been found convincing, essentially for the reasons of record as put forth in the Office Action mailed January 30, 2007.

Amendment of claim 23, and dependent claims thereof, to add the limitation "which can neutralize FGF-23 activity" does not serve to distinguish the claimed antibodies from the prior art antibodies of Itoh because the prior art antibodies of Itoh would inherently possess this property for the reasons of record essentially as put forth in the Office Action mailed January 30, 2007.

In particular, essentially as put forth in the Office Action mailed January 30, 2007, Itoh teaches FGF-23 is proteolytically cleaved into two fragments (1 to around 179 and around 180 to the C-terminal residue 251), that polyclonal or monoclonal antibodies can be generated against either fragment via "any suitable method known in the art...[f]or example, murine or human monoclonal antibodies can be produced by hybridoma technology...," and that said antibodies can be used for "preventing or treating diseases involving overexpression of the FGF-23 protein," such as "X-linked Hypophosphatemic rickets" (see Itoh page 18, 3rd to 4th paragraphs, page 30, 4th to 5th paragraphs and page 31, 3rd paragraph).

Given that the antibodies of Itoh bind the same sequence as the antibodies of the instant claims, i.e., amino acid 1to around 179 of FGF-23, and given that the antibodies of Itoh, like the instantly claimed antibodies, can be used to treat hypophosphatemic diseases involving overexpression of FGF-23, such as X-linked Hypophosphatemic rickets, and further given the highly conserved receptor binding surface of the FGF molecules, including FGF-23, as evidenced by Wu and Mohammadi (described in greater detail in the Office Action of January 30, 2007), the antibodies of Itoh would inherently compete with the instantly claimed antibodies.

Thus, the instant claims are anticipated by Itoh as evidenced by Yu and Mohammadi.

Since the Office does not have a laboratory to test the reference antibodies and determine if they compete with the instantly claimed antibodies, it is applicant's burden to show that the reference antibodies are not competitive with the instantly claimed antibodies. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald* et al., 205 USPQ 594 (CCPA 1980).

Applicant is reminded that as stated in MPEP § 2112.01, "[w]here the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada,* 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)."

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

   A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

   Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 23-25 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10 and 12-15 of copending USSN 10/344,339, in view of Yu et al. (Endocrinology. 2005 Nov;146(11):4647-56), Mohammadi et al. (Cytokine Growth Factor Rev. 2005 Apr;16(2):107-37), Bost et al. (Immunol. Invest. 1988; 17:577-586), essentially for the reasons of record as put forth in the Office Action mailed January 30, 2007.

   Applicant requests that this rejection be held in abeyance until allowable subject matter is indicated.

   Applicant's request is acknowledged, however, Applicant is advised that the instant rejection will be maintained until such time as a terminal disclaimer signed by the assignee and fully compliant with 37 CFR 3.73(b) is submitted.

8. Claims 23-25 stand directed to an invention not patentably distinct from claims 10 and 12-15 of commonly assigned USSN 10/344,339. Specifically, for the same reasons put forth above in the obviousness-type double patenting rejection.

Applicant asserts that "Copies of the company's regulation and the agreement between the employer and the employee(s) will be provided in a supplemental response to evidence the common ownership."

Applicant's assertion is acknowledged, however, Applicant is advised that a showing that the inventions were commonly owned at the time the invention in this application was made must be made in order to preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

The New Grounds of Rejection that follow were necessitated by applicant's amendment to the claims 22 and 25 to cancel "renal failure" the subject of the previous rejection under 35 U.S.C. § 112, 1st paragraph, put forth in the Office Action mailed January 30, 2007.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 22, 23 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody produced by FERM BP-7838, FERM BP-8268, FERM BP-7839 or FERM BP-7840, and a pharmaceutical composition of an antibody produced by FERM BP-7838, FERM BP-8268 and FERM BP-7839 where said pharmaceutical composition is effective against at least one disease selected from the group consisting of X-linked hypophosphatemic rickets, hypophosphatema and osteoporosis, and the particular complications of decreased renal function and hemodialysis, "renal osteodystrophy or dialysis osteopathy," or an antibody competitive with FERM BP-7838, FERM BP-8268, or FERM BP-7839 wherein said antibody neutralizes FGF-23 activity, and a pharmaceutical composition of an antibody competitive with the antibody produced by FERM BP-7838, FERM BP-8268 and FERM BP-7839 where said pharamaceutical composition is effective against at least one disease selected from the group consisting of X-linked hypophosphatemic rickets, hypophosphatema and osteoporosis, and the particular complications of decreased renal function and hemodialysis, "renal osteodystrophy or dialysis osteopathy," ***does not reasonably provide enablement for*** a pharmaceutical composition of an antibody produced by FERM BP-7840 where said pharmaceutical composition is effective against at least one disease selected from the group consisting of X-linked hypophosphatemic rickets, hypophosphatema and osteoporosis, and the particular complications of decreased renal function and hemodialysis, "renal osteodystrophy or dialysis osteopathy," or an antibody competitive with FERM BP-7840 wherein said antibody neutralizes FGF-23 activity, or a pharmaceutical composition of an antibody competitive with FERM BP-7840 where said pharamaceutical composition is effective against at least one disease selected from the group consisting of X-linked hypophosphatemic rickets, hypophosphatema and osteoporosis, and the particular complications of decreased renal function and hemodialysis, "renal osteodystrophy or dialysis osteopathy."

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The instant specification discloses that the FERM BP-7840 antibody binds to the C-terminal amino acid residues 237-251 of FGF-23 (see, in particular, instant specification page 17).

However, apart from binding to the C-terminus of FGF-23, the instant specification does not exemplify any other biological activity for the FERM BP-7840 antibody.

Moreover, there is reason to believe that the FERM BP-7840 antibody binds to the C-terminal amino acid residues 237-251 of FGF-23 or an antibody that competes with said antibody would not have the ability to neutralize FGF-23 activity or to be effective as a pharamaceutical composition against at least one disease selected from the group consisting of X-linked hypophosphatemic rickets, hypophosphatema and osteoporosis, and the particular complications of decreased renal function and hemodialysis, "renal osteodystrophy or dialysis osteopathy," because according to Yu et al. (Endocrinology. 2005 Nov;146(11):4647-56, cited previously), FGF-23 binds to FGF receptors 1c, 2c, 3c and 4 (see entire document, in particular Discussion pages 4652-4655) and according to Mohammadi et al. (Cytokine Growth Factor Rev. 2005 Apr;16(2):107-37, cited previously), FGF polypeptides, including FGF-23, bind to FGF receptors via a conserved set of residues that are found within amino acids 1 to 179 of FGF-23, and these residues are primarily found along one face of the FGF conserved β-trefoil core (see, part 1-2, pages 107-120, in particular Figures 1 and 5).

Given that the FERM BP-7840 antibody does not bind to the portion of FGF-23 known to interact with the FGF receptors, it is highly unlikely that the FERM BP-7840 antibody will neutralize FGF-23, or a pharmaceutical composition comprising the FERM BP-7840 antibody or a pharmaceutical composition comprising an antibody that competes with said antibody will be effective against at least one disease recited in the instant claims.

The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Thus, the instant claims are not enabled under 35 U.S.C. § 112, 1st paragraph.

11. Claims 20 and 21 are allowable.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until

after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary Skelding whose telephone number is 571-272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Zachary Skelding, Ph.D.
Patent Examiner
October 4, 2007

MICHAIL BELYAVSKYI, PH.D.
PATENT EXAMINER

10/05/07